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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,588	08/20/2003	Connie Sanchez	05432/100M919-US3	5265

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DARBY & DARBY P.C.
P. O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER	
LEWIS, AMY A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,588	SANCHEZ ET AL.	
	Examiner	Art Unit	
	Amy A. Lewis	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S:10

DETAILED ACTION

Status of the Case

The Preliminary Amendment, filed 5 January 2004, has been entered into the application. Accordingly, claims 1-19 have been cancelled, and new claims 20-37 have been added.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on Application PCT/DK02/00281, filed 1 May 2002, and PA 2001 00684 filed in Denmark on 1 May 2001. It is noted, however, that applicant has not filed a certified copy, and certified English language translation, of the applications as required by 35 U.S.C. 119(b). Therefore, this application will be examined according to the priority date of 20 August 2003 (the current filing date).

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a non-provisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1) Claims 22, 23, 28, 29, 34, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "to obtain an effect" in claims 22 and 23 is a relative term which renders the claim indefinite. The term " to obtain an effect " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to what "effect" is to be obtained, nor what change or how much of a change is considered to be "an effect" in the patient.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1) Claims 20, 22, 24-28, 30-34, 36 and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 40-46 of copending Application No. 10/468,685 (Pub. No. US 2004/0198809 A1). Although the conflicting claims

are not identical, they are not patentably distinct from each other because they are both directed to a method of treating depression in a patient in need thereof, comprising administering a pharmaceutically effective amount of escitalopram or a pharmaceutically acceptable salt thereof (particularly the oxalate salt or crystalline oxalate salt) to the patient, wherein the daily dose is 10 mg or less. The '685 co-pending application is directed to treating major depressive disorder and the instant application is directed to treating severe depression (a subclass of major depressive disorder). This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

2) Claims 21, 23, 29, and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 40-46 of Application No. 10/468,685 (Pub. No. US 2004/0198809 A1), in view of Gorman JM, et al. ("Efficacy comparison of escitalopram and citalopram in the treatment of major depressive disorder: pooled analysis of placebo-controlled trials," 2002 April *CNS Spectr.* 7(4 Suppl 1): 40-44).

The conflicting claims are both directed to a method of treating depression in a patient in need thereof, comprising administering a pharmaceutically effective amount of escitalopram or a pharmaceutically acceptable salt thereof (particularly the oxalate salt or crystalline oxalate salt) to the patient, wherein the daily dose is 10 mg or less. The '685 application is directed to treating major depressive disorder and the instant application is directed to treating severe depression (a subclass of major depressive disorder). The '685 co-pending application does not recite the limitation of a MADRS score of at least 29 (of claims 21, 23, 29, and 35).

The Gorman et al. reference teaches that depressed patients had a minimum MADRS score of 22 ("Patients" section on p. 41), severely depressed was defined as a MADRS score of ≥ 30 (p. 43, 3rd paragraph), and that the mean baseline score for patients in the study was a MADRS score of 29 (p. 43, last paragraph). It would have been obvious to one of ordinary skill in the art to use escitalopram in a method of treating patients with severe depression and a MADRS score of at least 29, having been taught by Gorman that patients that score 30 on the MADRS test are classified as having depressive disorder/severe depression.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

3) Claims 20, 22, 24-28, 30-34, 36 and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 20-40 of copending Application No. 10/644,579 (Pub. No. US 2004/0192765 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both directed to a method of treating depression in a patient in need thereof, comprising administering a pharmaceutically effective amount of escitalopram or a pharmaceutically acceptable salt thereof (particularly the oxalate salt or crystalline oxalate salt) to the patient, wherein the daily dose is 10 mg or less. The '579 co-pending application is directed to treating depression in a patient who failed to respond to initial treatment with a selective serotonin reuptake inhibitor (other than escitalopram) and the instant application is directed to treating severe depression (a subclass of major depressive disorder). This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

4) Claims 21, 23, 29, and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-40 of copending Application No. 10/644,579 (Pub. No. US 2004/0192765 A1), in view of Gorman JM, et al. "Efficacy comparison of escitalopram and citalopram in the treatment of major depressive disorder: pooled analysis of placebo-controlled trials," 2002 April *CNS Spectr.* 7(4 Suppl 1): 40-44.

The conflicting claims are both directed to a method of treating depression in a patient in need thereof, comprising administering a pharmaceutically effective amount of escitalopram or a pharmaceutically acceptable salt thereof (particularly the oxalate salt or crystalline oxalate salt) to the patient, wherein the daily dose is 10 mg or less. The '579 co-pending application is directed to treating depression in a patient who failed to respond to initial treatment with a selective serotonin reuptake inhibitor (other than escitalopram) and the instant application is directed to treating severe depression (a subclass of major depressive disorder). The '579 co-pending application does not recite the limitation of a MADRS score of at least 29 (of claims 21, 23, 29, and 35).

The Gorman et al. reference teaches that depressed patients had a minimum MADRS score of 22 ("Patients" section on p. 41), severely depressed was defined as a MADRS score of $\geq$ 30 (p. 43, 3rd paragraph), and that the mean baseline score for patients in the study was a MADRS score of 29 (p. 43, last paragraph). It would have been obvious to one of ordinary skill in the art to use escitalopram in a method of treating patients with severe depression and a

MADRS score of at least 29, having been taught by Gorman that patients that score 30 on the MADRS test are classified as having depressive disorder/severe depression.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1) Claims 20-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorman JM, et al. "Efficacy comparison of escitalopram and citalopram in the treatment of major depressive disorder: pooled analysis of placebo-controlled trials," 2002 April *CNS Spectr.* 7(4 Suppl 1): 40-44. Burke WJ et al. ("Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients," *J Clin Psychiatry* 2002 April; 63(4): 331-336) is viewed as an equivalent teaching.

Gorman et al. teaches escitalopram (the S-isomer of citalopram), as compared to placebo, at doses of 10-20 mg/day (claim 20, 24 and 25) is effective and well tolerated in the treatment of major depressive disorder (see current claim 20), including severe depression (p. 40, abstract & introduction). Patients were evaluated on the MADRS test at the end of week 4 or week 6 of the study (which meets the limitations of claims 21-23, regarding an effect after one week and the MADRS score). The Gorman et al. reference teaches that depressed patients had a minimum

MADRS score of 22 ("Patients" section on p. 41), severely depressed was defined as a MADRS score of $\geq$ 30 (p. 43, 3rd paragraph), and that the mean baseline score for patients in the study was a MADRS score of 29 (p. 43, last paragraph).

2) Claims 20and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Boegesoe et al. (US Pat. 4,943,590).

Boegesoe et al. teach (+)-citalopram (which is escitalopram) for the treatment of depression (current claim 20). The reference teaches "a method for alleviating depression in a living animal body subject thereto" by administering an effective amount of the compound or pharmaceutically acceptable salts (which is escitalopram), at dosages ranging from 0.10-100 mg and preferably 5-50 mg daily (current claim 24). (See: abstract; col. 8 Table 1; col. 8, lines 55-66; claims 1-2 & 7-12).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1) Claims 20, 24, 26, 28, 30, 32, 34, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boegesoe et al. (US Pat. 4,943,590) in view of Bilski et al. (US Pat. 4,764,361).

Boegesoe et al. teach (+)-citalopram (which is escitalopram) for the treatment of depression (current claim 20). The reference teaches "a method for alleviating depression in a living animal body subject thereto" by administering an effective amount of the compound or pharmaceutically acceptable salts (which is escitalopram), at dosages ranging from 0.10-100 mg and preferably 5-50 mg daily (current claim 24). (See: abstract; col. 8 Table 1; col. 8, lines 55-66; claims 1-2 & 7-12).

Bilski et al. teaches the oxalate and crystalline oxalate salts of the (S) isoform of a racemic mixture. The reference does not teach escitalopram.

It would have been obvious to one of ordinary skill in the art to use the oxalate or crystalline oxalates salt of escitalopram in the instantly claimed method of treating severe depression, having been taught by the prior art that it is known to make oxalate and crystalline oxalate salts of a racemic compound to obtain the (S) isoform and motivated by the desired to obtain an optically active (S) isoform salt of citalopram (i.e. escitalopram).

2) Claims 20-25, 27, 29, 31, 33, 35, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorman JM, et al. ("Efficacy comparison of escitalopram and citalopram in

the treatment of major depressive disorder: pooled analysis of placebo-controlled trials," 2002 April *CNS Spectr.* 7(4 Suppl 1): 40-44) in view of Bilski et al. (US Pat. 4,764,361).

Gorman et al. teaches escitalopram (the S-isomer of citalopram), as compared to placebo, at doses of 10-20 mg/day (claim 20, 24 and 25) is effective and well tolerated in the treatment of major depressive disorder (see current claim 20), including severe depression (p. 40, abstract & introduction). Patients were evaluated on the MADRS test at the end of week 4 or week 6 of the study (which meets the limitations of claims 21-23, regarding an effect after one week and the MADRS score). The Gorman et al. reference teaches that depressed patients had a minimum MADRS score of 22 ("Patients" section on p. 41), severely depressed was defined as a MADRS score of $\geq$ 30 (p. 43, 3rd paragraph), and that the mean baseline score for patients in the study was a MADRS score of 29 (p. 43, last paragraph)

Bilski et al. teaches the oxalate and crystalline oxalate salts of the (S) isoform of a racemic mixture. The reference does not teach escitalopram. Again, Hertel et al. (US Pat. 6,353,008 B1), viewed as an equivalent teaching to Bilski.

It would have been obvious to one of ordinary skill in the art to use the oxalate or crystalline oxalates salt of escitalopram in the instantly claimed method of treating severe depression, having been taught by the prior art that it is known to make oxalate and crystalline oxalate salts of a racemic compound to obtain the (S) isoform and motivated by the desired to obtain the active (S) isoform salt of citalopram (i.e. escitalopram).

Pertinent Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

- Burke WJ et al. "Fixed-dose trial of the single isomer SSRI escitalopram in depressed outpatients," *J Clin Psychiatry* 2002 April; 63(4): 331-336, which teaches treatment of major depressive disorder with 10mg/day and 20mg/day of escitalopram and evaluation based on the MADRS scale. This reference is viewed as an equivalent to the Gorman et al. reference.
- Montgomery & Asberg ("A new depression scale designed to be sensitive to change," *Br J Psychiatry* 1979; 134: 382-389), which teaches the MADRS scale.
- Hertel et al. (US Pat. 6,353,008 B1), viewed as an equivalent teaching to Bilski, also teaches a method of obtaining the desired isoform of a racemic compound (specifically serotonin reuptake inhibitors) by converting the crude free base of a compound to an oxalate salt and recrystallizing to obtain the purified compound (see abstract; col. 11, line 55-col. 12, line 8; col. 17, lines 50- col. 18, line 67).

Contact Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy A. Lewis whose telephone number is (571) 272-2765. The examiner can normally be reached on Monday-Friday, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy A. Lewis
Patent Examiner
Art Unit 1614

Amy Lewis

Christopher Low
SPE
Art Unit 1614

Christopher S.F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600